

REMARKS

Favorable action on the merits is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS & AMENDMENTS

Claims 1-36 were pending in this application when last examined.

Claims 1-22 have been examined and stand rejected.

Claims 23-36 have been withdrawn as non-elected subject matter.

Claims 1 and 20 have been amended to clarify the nucleotide corresponding to the recited "3' terminal" and to identify the location of the two bases on the uncomplementary regions. Support for these changes can be found in the disclosure, for example, at page 12, lines 20-25 and page 40, lines 14-16 and original claims 1 and 20. Other minor editorial changes have been made to claims 1 and 20 to better conform with US practice and to correct minor grammatical and punctuation errors. Support can be found in the claims as filed.

Claim 12 has been amended to recite "includes" before "diaphorase" to use the proper plural form of the verb. Support can be found in the claim as filed.

Therefore, no new matter has been added by this amendment to the claims.

II. FOREIGN PRIORITY

In item 3 on page 2 of the Action, the foreign priority claim was denied on the basis that certified "translations" of the priority documents have not been received.

This position is respectfully traversed.

Generally, to establish foreign priority, it is sufficient to submit a claim for priority along with a certified copy of the foreign application. See 37 C.F.R. § 1.55(a)(1)-(2) and M.P.E.P. § 201.14(a)-(b). Certified "translations" of the priority documents are only required to establish priority to overcome a prior art rejection over intervening art. See 37 C.F.R. § 1.55(a)(4) and M.P.E.P. § 201.14(a).

In this case, there is no prior art rejection using intervening. Moreover, both a claim for foreign priority (*i.e.*, the Oath/Declaration) and certified copies of the priority documents were submitted with the filing of this application. In this regard, kindly note that the indication in item 12(a)1 on page 1 of the Action, wherein it is indicated that the claim for foreign priority has been acknowledged along with receipt of the certified priority document. Therefore, it is unnecessary to submit certified "translations" of the priority documents to establish priority in this case.

For these reasons, it is respectfully submitted that the requirements to establish foreign priority have been met.

Therefore, kindly acknowledge the claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f), as well as receipt of the certified copies of the foreign priority document.

III. INFORMATION DISCLOSURE STATEMENT

An Examiner-initialed copy of the Form PTO 1449 submitted with the IDS dated December 5, 2003 was attached to the Office Action in which reference AH (JP 2001-57892) and reference AK (JP 2002-101899) were not considered.

Presumably, reference AK was lined through as it was cited and considered in the Notice of References Cited (Reference O, JP 2002-101899). However, it is unclear why reference AH (JP 2001-57892) was lined through. Therefore, kindly consider reference AH and return an Examiner-initialed copy of the Form PTO 1449 indicating such, or clarify why the reference was not considered.

IV. DOUBLE PATENTING REJECTIONS

In item 5 on pages 3-7, claims 1-9, 14-17 and 19 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as obvious over claims 1, 3, 4 and 6 of copending Application No. 11/180,881 in view of Sorenson (WO 93/22456) and Kambara et al. (JP 2002-101899).

In item 6 on pages 7-9, claim 18 was provisionally rejected on the ground of nonstatutory obviousness-type double patenting as obvious over claims 1, 3, 4 and 6 of copending Application No. 11/180,881 in view of Sorenson and Kambara, and further in view of Morad (US 4,894,376).

In item 7 on pages 9-13, claims 1-13 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as obvious over claims 2, 3, 5 and 6 of copending Application No. 10/699,848 in view of Sorenson and Kambara.

Without intending to acquiesce to these rejections and merely to expedite allowance of the application, the Applicants submit herewith a Terminal Disclaimer under 37 C.F.R. § 1.321, which is signed by a registered attorney of record, together with the fee required under 37 C.F.R. § 1.20(d) to overcome the obviousness-type double patenting rejections over co-pending Application Nos. 11/180,881 and 10/699,848. The Terminal Disclaimer removes these applications as references.

Therefore, the double patenting rejections are untenable and should be withdrawn.

V. INDEFINITENESS REJECTION

In item 9 on page 13, claims 1-22 were rejected under 35 U.S.C. § 112, second paragraph, as indefinite for the phrase “3’ terminal” in claims 1 and 20.

It is respectfully submitted that the present amendment overcomes this rejection.

As noted above, claims 1 and 20 have been amended to clarify the nucleotide corresponding to the recited “3’ terminal” as supported by the disclosure, for example, at page 12, lines 20-25 and page 40, lines 14-16 and original claims 1 and 20. It is respectfully submitted that one of skill in the art, upon reading the disclosure and in view of the knowledge in the art, would understand the metes and bounds of the claimed language in view of this amendment.

Therefore, the rejection of claims 1-22 under 35 U.S.C. § 112, second paragraph, is untenable and should be withdrawn.

VI. OBVIOUSNESS REJECTIONS

In item 12 on pages 14-16, claims 1-6, 9, 20 and 21 were rejected under 35 U.S.C. § 103(a) as obvious over Sorenson.

In item 13 on pages 16-17, claims 7 and 8 were rejected under 35 U.S.C. § 103(a) as obvious over Sorenson in view of Kambara.

In item 14 on pages 17-18, claim 22 was rejected under 35 U.S.C. § 103(a) as obvious over Sorenson in view of Newton (US 5,525,494).

In item 15 on pages 18-20, claims 14-19 were rejected under 35 U.S.C. § 103(a) as obvious over Sorenson in view of Kambara and Bille et al. (Phys. Plantarum, Vol. 84, pp. 250-254 (1992)).

These rejections are respectfully traversed as applied to the amended claims.

Since Sorenson is the primary reference in all of the rejections, these rejections will be discussed herein together.

Claims 1 and 20 have been amended to specify that the two bases in the “uncomplementary region” (claim 1) and “second uncomplementary region” (claim 20) are located in the second and third positions from the 3' terminal of the first single-stranded nucleic acid.

The Office has indicated that it would have been obvious to one of ordinary skill in the art to arrive at the present invention of claims 1-6, 9, 20 and 21 based on Sorenson's teaching, at page 16, lines 1-3, that allele specific primers can have some mismatches 3-6 nucleotides from a 3' end that would not be likely to interfere with efficacy (of SNP detection).

However, such a disclosure is not a suggestion for having two bases in the “uncomplementary region” (claim 1) and “second uncomplementary region” (claim 20) that are located in the second and third positions from the 3' terminal of the first single-stranded nucleic acid as in the present invention.

In this regard, the base type determination primer as recited in amended claim 1 is different from the primer disclosed in Sorenson. Again, the amended claims call for a base at the

third position from the 3' terminal of the base type determination primer, and, especially, a base in the second position from 3' terminal of the primer, which are uncomplementary to one strand of a target double-stranded nucleic acid. It is respectfully submitted that Sorenson fails to disclose or suggest this element of the invention of the amended claims.

Likewise, the secondary references of Kambara, Newton and Bille also fail to disclose or suggest this element of the invention of the amended claims.

Therefore, the cited references cannot render the claimed invention obvious, because they fail to disclose or suggest each and every element of the invention.

Furthermore, the present invention is believed to be patentable over the cited references in view of the unexpected and superior results achieved by the present invention. Such results are indicative of non-obviousness.

In the base type determination method as recited in amended claim 1, the second base from the 3' terminal of the primer, which is uncomplementary to one strand of the target double-stranded nucleic acid, causes a remarkable decrease in incorrect determination of a base in a substituted region, i.e., SNP site (determination of pseudo-positive).

Attached herewith is a description of five experiments, which were performed by the Applicants, and demonstrate the superiority of the present invention over the prior art. See the attached five experiments (First Experiment - Fifth Experiment) (pages 1-23, including Figs. 1-5).

Applicants will submit and executed Rule 132 Declaration discussing the attached experiments in due course.

The attached experiments demonstrate a clear difference between the present invention over the prior art. In particular, the results therein are evidence that the allele-specific primers according to the present invention achieve a significantly superior pseudo-positive repression effect over the prior art allele specific primers as represented by Sorenson.

In particular, in Figs. 1-5 of the supplementary experimental data, each of the vertical scales represents "a concentration of amplified products" or "a ratio of fluorescence intensity",

which indicates occurrence of incorrect determination of a base in a substituted region (determination of pseudo-positive). In other words, the higher the concentration of amplified products or the ratio of fluorescence intensity is, the more the incorrect determination (determination of pseudo-positive) occurs.

In the attached experiments, the following samples correspond to the prior art primers:

Samples (1-1) to (1-3) in the First Experiment (paragraph bridging pages 1-2),
Samples (2-1) to (2-3) in the Second Experiment (last paragraph on page 5),
Samples (3-1) to (3-3) in the Third Experiment (paragraph bridging pages 9-10),
Samples (4-1) to (4-3) in the Fourth Experiment (paragraph bridging pages 13-14), and
Samples (5-1) to (5-3) in the Fourth Experiment (page 18).

In the attached experiments, the following samples correspond to the allele-specific primers according to the present invention:

Samples (1-4) to (1-8) in the First Experiment (paragraph bridging pages 1-2),
Samples (2-4) to (2-8) in the Second Experiment (last paragraph on page 5),
Samples (3-4) to (3-8) in the Third Experiment (paragraph bridging pages 9-10),
Samples (4-4) to (4-8) in the Fourth Experiment (paragraph bridging pages 13-14), and
Samples (5-4) to (5-8) in the Fourth Experiment (page 18).

The results of these experiments clearly show that when a base in the second position from 3' terminal end of the primer is complementary to a target nucleic acid, as in samples (1-1) to (1-3), (2-1) to (2-3), (3-1) to (3-3), (4-1) to (4-3) and (5-1) to (5-3) (as in the prior art), the concentration of amplified products is equal to or greater than 100nM and the ratio of fluorescence intensity is equal to or greater than 50%.

In contrast, when a base in the second position from the 3' terminal end of the primer is uncomplimentary to a target sequence, as in samples (1-4) to (1-8), (2-4) to (2-8), (3-4) to (3-8), (4-4) to (4-8) and (5-4) to (5-8) (as in the present invention), the concentration of amplified products and the ratio of fluorescence intensity are substantially zero.

These results highlight a clear difference between the allele specific primers of the present invention and those in the prior art.

Referring back to the primary reference, Sorenson discloses an SNP detecting method. However, Sorenson merely discloses that the allele specific primers can have some mismatches 3-6 nucleotides, *i.e.*, at the third to sixth base position, from the 3' terminus that would not be likely interfere with efficacy of SNP detection. In other words, while Sorenson teaches that a base third from 3' end may be uncomplimentary to a target nucleic acid, there is no disclosure or suggestion in the reference that a base in the second position from 3' end may be uncomplimentary to the target nucleic acid of the amended claims. In particular, Sorenson fails to disclose or suggest that the base in the second position from 3' terminal of the primer is uncomplimentary to the target nucleic acid. Therefore, it would not have been obvious to one of ordinary skill in the art at the time the invention was made to attain the above-mentioned remarkable effect achieved by the present invention in view of the teaching in Sorenson.

Furthermore, the secondary references of Kambara, Newton and Bille references also fail to disclose or suggest the above-noted features of the present invention as recited in claim 1. For example, while Kambara (JP 2002-101899) discloses in Fig. 1 a primer having a base third from 3' terminal complementary to a target nucleic acid, there is no disclosure or suggestion of a base in the second position from the 3' terminal end, as well as a base in the third position from 3' terminal end, that is uncomplementary to the target nucleic acid. Likewise, Newton relates generally to labeling primers, and Bille relates to a study of sphingosine as an inhibitor of protein kinase C. Neither reference mentions anything about bases in the second and third positions from the 3' terminal end that are uncomplementary to the target nucleic acid.

In view of the foregoing, it is respectfully submitted that the cited references, taken alone or in combination, fail to disclose or suggest each and every element of the claimed invention, and the present invention achieves superior and unexpected results over the prior art. Therefore, the above-noted prior art rejections are untenable and should be withdrawn.

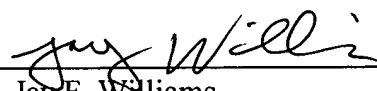
CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Hidenobu YAKU et al.

By: 
Jay F. Williams
Registration No. 48,036
Attorney for Applicants

JFW/akl
Washington, D.C. 20006-1021
Telephone (202) 721-8200
Facsimile (202) 721-8250
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ATTACHMENTS

1. Terminal Disclaimer;
2. Descriptions of five experiments (First Experiment - Fifth Experiment) (pages 1-23, including Figs. 1-5).